



cerebral folate transport deficiency

Cerebral folate transport deficiency is a disorder that develops from a shortage (deficiency) of the B-vitamin folate (also called vitamin B9) in the brain. Affected children have normal development during infancy, but around age 2 they begin to lose previously acquired mental and movement abilities (psychomotor regression). They develop intellectual disability, speech difficulties, and recurrent seizures (epilepsy). Movement problems such as tremors and difficulty coordinating movements (ataxia) can be severe, and some affected individuals need wheelchair assistance. Affected individuals have leukodystrophy, which is a loss of a type of brain tissue known as white matter. White matter consists of nerve fibers covered by a fatty substance called myelin that promotes the rapid transmission of nerve impulses. Leukodystrophy contributes to the neurological problems that occur in cerebral folate transport deficiency. Without treatment, these neurological problems worsen over time.

Frequency

The prevalence of cerebral folate transport deficiency is unknown. Fewer than 20 affected individuals have been described in the scientific literature.

Genetic Changes

Mutations in the *FOLR1* gene cause cerebral folate transport deficiency. The *FOLR1* gene provides instructions for making a protein called folate receptor alpha. This protein is found within the cell membrane where it attaches (binds) to folate, allowing the vitamin to be brought into the cell. Folate receptor alpha is produced in largest amounts in the brain, specifically in an area of the brain called the choroid plexus. This region releases cerebrospinal fluid (CSF), which surrounds and protects the brain and spinal cord. Folate receptor alpha is thought to play a major role in bringing folate from the bloodstream into brain cells. It transports folate across the choroid plexus and into the CSF, ultimately reaching the brain. In the brain, folate is needed for making myelin and chemical messengers called neurotransmitters. Both of these substances play essential roles in transmitting signals in the nervous system. Additionally, folate is involved in the production and repair of DNA, regulation of gene activity (expression), and protein production.

FOLR1 gene mutations result in a lack of protein or malfunctioning protein. As a result, folate from the bloodstream cannot be transported into the CSF. Without folate, many processes in the brain are impaired, leading to the neurological problems typical of cerebral folate transport deficiency.

The signs and symptoms of cerebral folate transport deficiency do not begin until late infancy because other mechanisms can compensate for this loss. For example, another protein called folate receptor beta is responsible for folate transport before birth and in early infancy.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- cerebral folate deficiency
- FOLR1 deficiency
- neurodegeneration due to cerebral folate transport deficiency

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Cerebral folate deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2751584/>

Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Folic Acid--Test
<https://medlineplus.gov/ency/article/003686.htm>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Folate Deficiency
<https://medlineplus.gov/ency/article/000354.htm>
- Encyclopedia: Folic Acid--Test
<https://medlineplus.gov/ency/article/003686.htm>
- Health Topic: Developmental Disabilities
<https://medlineplus.gov/developmentaldisabilities.html>
- Health Topic: Folic Acid
<https://medlineplus.gov/folicacid.html>
- Health Topic: Leukodystrophies
<https://medlineplus.gov/leukodystrophies.html>
- Health Topic: Speech and Language Problems in Children
<https://medlineplus.gov/speechandlanguageproblemsinchildren.html>

Genetic and Rare Diseases Information Center

- Cerebral folate deficiency
<https://rarediseases.info.nih.gov/diseases/10594/cerebral-folate-deficiency>

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Epilepsy Information Page
<https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page>
- NIH Office of Dietary Supplements: Folate
<https://ods.od.nih.gov/factsheets/Folate-HealthProfessional/>

Educational Resources

- Centers for Disease Control and Prevention: Facts About Developmental Disabilities
<https://www.cdc.gov/ncbddd/developmentaldisabilities/facts.html>
- Centers for Disease Control and Prevention: Folic Acid
<https://www.cdc.gov/ncbddd/folicacid/index.html>
- Cleveland Clinic: Leukodystrophy
<http://my.clevelandclinic.org/health/articles/leukodystrophy>
- Disease InfoSearch: Neurodegeneration due to cerebral folate transport deficiency
<http://www.diseaseinfosearch.org/Neurodegeneration+due+to+cerebral+folate+transport+deficiency/5162>

- Kennedy Krieger Institute: Developmental Disorders
<https://www.kennedykrieger.org/patient-care/diagnoses-disorders/developmental-disorders>
- Kennedy Krieger Institute: Leukodystrophy
<https://www.kennedykrieger.org/patient-care/diagnoses-disorders/leukodystrophy>
- KidsHealth from Nemours: Delayed Speech or Language Development
<http://kidshealth.org/en/parents/not-talk.html>
- MalaCards: cerebral folate deficiency
http://www.malacards.org/card/cerebral_folate_deficiency
- Merck Manual Home Edition for Patients and Caregivers: Folate
<http://www.merckmanuals.com/home/disorders-of-nutrition/vitamins/folate>
- Orphanet: Neurodegenerative syndrome due to cerebral folate transport deficiency
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=217382
- Seattle Children's Hospital: Epilepsy Symptoms and Diagnosis
<http://www.seattlechildrens.org/medical-conditions/brain-nervous-system-mental-conditions/epilepsy-symptoms/>

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
<http://aaid.org/>
- CURE Epilepsy
<http://www.cureepilepsy.org/home.asp>
- Resource List from the University of Kansas Medical Center: Developmental Delay/Mental Retardation
<http://www.kumc.edu/gec/support/devdelay.html>
- The Arc: For People with Intellectual and Developmental Disabilities
<http://www.thearc.org/>
- United Leukodystrophy Foundation
<http://ulf.org/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28FOLR1%5BTIAB%5D%29+AND+%28cerebral+folate+deficiency%5BTIAB%5D%29+OR+%28cerebral+folate+transport+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- **NEURODEGENERATION DUE TO CEREBRAL FOLATE TRANSPORT DEFICIENCY**
<http://omim.org/entry/613068>

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